

preparing a different isotopic spike for each species to be measured by converting each said stable isotope to a speciated enriched isotope corresponding to the species to be measured in said sample,

spiking the sample containing said species to be measured,

equilibrating said isotopic spiked species with said species to be measured,

separating only a portion of said species from said sample in order to effect incomplete separation,

making isotope ratio determinations for each said species to be measured and mathematically deconvoluting said species concentration while correcting for species conversion, and

effecting said mathematical deconvolution while correcting for said incomplete separation of said species from said sample.

10. (Amended) The method of speciated isotope dilution measurement of Claim 2 including

employing said process on a plurality of said species to be measured, and incompletely separating said species from other said species in said sample.

#### REMARKS

In response to the final Office Action dated December 18, 2001, in the captioned CPA, the application has been reviewed carefully and the application amended in a sincere effort to place the same in condition for allowance. Reconsideration of the prior rejection and allowance of the remaining amended claims are respectfully requested on the basis of the following remarks.

#### THE INVENTION

The present invention has solved a number of problems in respect of existing procedures for isotope dilution mass spectrometry through the creation of speciated isotope dilution mass spectrometry which has capabilities above and beyond the existing state of the art in the former practices. The present invention provides for mathematical deconvolution of the species concentration while correcting for species conversion and incomplete separation of the species from the sample. It also provides for species by species

determination of concentration and for the creation of standards for use in such determinations.

These features among others are discussed throughout the specification including the extensive examples, which contain comparative data and confirmation of the operability of applicant's invention. See the examples beginning at the top of page 17 through page 45, line 10.

Table II, which appears at the top of page 31 and the discussion regarding the same which begins at line 21 on page 31, provides an analysis of the successful performance of the SIDMS (speciated isotope dilution mass spectrometry) of the present invention along with a comparison contained in the last two columns of conventional isotope dilution mass spectrometry. Columns 9 and 10 of Table II, which columns bear the heading "Conventional IDMS" lists the results of using the IDMS approach contained in column 2 with resultant systemic errors as contrasted with the ability to correct for species conversion in addition to improving the precision and detection limits of the presently claimed invention.

Amended claim 1, which is the sole independent claim in the application, clearly recites these distinguishing characteristics of the invention. More specifically, it is directed toward a method of speciated isotope dilution measurement of a sample which includes providing at least one predetermined stable isotope and preparing a different isotopic spike for each species to be measured by converting each stable isotope to a speciated enriched isotope corresponding to the species to be measured in the sample. The sample containing the species to be measured is spiked and equilibrating of the isotope-spiked species with the species to be measured is then performed.

The Examiner's astute observation regarding the expression dealing with separation of "at least a portion" of said species from the sample has been noted with appreciation. The claim has been amended so as to emphasize the fact that the process is to be contrasted with the cited prior Kingston patent (U.S. Patent 5,414,259.) It recites separating only a portion of said species from said sample in order to effect incomplete separation. Isotope ratio determinations are made for each species to be measured and mathematically deconvoluting the species concentration while correcting for species conversion and effecting mathematical deconvolution while correcting for incomplete separation of the

species from the sample. As will be discussed hereinafter, the dependent claims further refine the method.

**Claim 4 – Section 112, Paragraph 2**

This claim has been cancelled, thereby obviating this ground of rejection.

**Claims 1-3, 5-33 – Section 102(b)**

These claims were all rejected on the basis of Kingston U.S. Patent 5,414,259.

Claim 1, which is the sole independent claim in the group has been amended so as to distinguish over the teaching of the prior Kingston patent. The present invention as set forth in amended claim 1 now recites that separation of only a portion of the species from the sample is effected in order to provide for incomplete separation with subsequent correction being provided therefor. The prior Kingston patent contemplates separation of the entire species from the sample. See, for example, column 7, lines 29-38; column 13, lines 63-65, column 14, lines 5-9 and claim 1, which recites "separating all said species from said sample." This distinction represents a significant advancement of the presently claimed Kingston invention over his prior cited patent.

Reference to the present invention shows support in the examples on pages 41-47 and related Figures 8, 9(a) and 9(b). It is this capability to provide adequate quantitative data without requiring efficient extraction of the species from the sample that is a significant portion of the presently disclosed and claimed invention, which is not taught or suggested by Kingston '259.

Dependent claim 2 recites employing the method on more than one species simultaneously and dependent claim 3 recites quantification of Cr(III) and Cr(VI).

The feature of claim 5 is claimed solely in the context of amended claim 1 from which it depends.

Claim 6 recites tagging the enriched isotope with an isotopic tag in the same speciated form as the species to be measured and claim 7 recites employing time resolution chromatography to effect said separation.

Dependent claim 8 recites employing the process on a sample, which has experienced species conversion prior to separation.

Claim 9 recites effecting equilibrium in an aqueous solution.

Claim 10 as amended recites employing the process on a plurality of said species to be measured and incompletely separating said species from other said species in said sample. This is inconsistent with the teaching of the cited Kingston reference. This formed no part of the original cited patent and is supported by data contained in Figures 9(a) and 9(b), and the related above-referenced examples. This portion of the method facilitates accomplishing a precise and accurate result on what otherwise might be considered an inadequate specimen.

Dependent claim 11, which depends from claim 3, recites effecting the separation after reduction of a substantial portion of Cr(VI) to Cr(III). Claim 12 recites employing the method on a soil sample and claim 13 recites employing it on an aqueous sample. Claim 14 recites employing the process on solid waste from a chromite ore processing system. Solid samples present a different dimension of problem.

Claim 15 expressly recites storing the sample after the equilibrating step and prior to the separation step.

Dependent claim 16 recites effecting mathematical deconvoluting simultaneously with respect to more than one species to be measured. Claim 17, which depends from claim 16, recites effecting the mathematical deconvolution for each species independently of the other species.

Claim 18 depends from claim 1 and recites deconvoluting with respect to only one species to be measured.

Claim 19 depends from claim 16 and recites effecting the separation of at least about 5 to 10 percent less than 100 percent of each species from the sample and from the other species before effecting deconvolution. There is no such teaching or suggestion in the cited reference.

Claim 20, which depends from claim 1, recites preferred methods of separation employed in the context of the method of claim 1.

Claim 21 recites effecting the separation by microwave assisted extraction for a period of about 5 to 15 minutes. There is no such teaching in the cited reference. The data supporting this is discussed in the specification with respect to the Figure 10.

Claim 22, which depends from claim 21, recites effecting the separation at about 90° C to 150° C. These preferred approaches were not part of the cited reference.

Dependent claim 23 recites the method employed for purposes of validating another type of test. This is not taught or suggested by the cited reference.

Claim 24, which depends from 23, recites effecting a plurality of measurements by the other tests and effecting the comparison in evaluating the validity of the other tests.

Claim 25 recites a significant advancement in connection with the creation of speciated spiked standard materials. This subject was not dealt with at all in the cited Kingston patent.

Claim 26 depends from claim 1 and recites employing the method to prepare standard materials.

Claim 27, which depends from claim 25, recites the creation of the new standards spiked with isotopically enriched species in different forms.

Claim 28, which depends from claim 26, recites employing the standard materials after storage. The cited reference did not deal with such concepts.

Claim 29, which depends from claim 26, recites employing the method to correct species shifts in the standard material after degradation.

Claim 30, which depends from claim 21, recites employing in the microwave extraction closed vessel microwave extraction.

Dependent claim 31, which depends from claim 23, recites the contribution of the method validating tests, which are “not independently capable of compensating for incomplete species extraction or species conversion.” The specification discussion regarding Figures 9(a) and 9(b) is related to this feature, as is the specification discussion at page 44, line 17 through page 45, line 10.

Dependent claim 32 recites performing the method on a species, which due to incomplete separation, loss, conversion, or degradation has less than 100 percent of this species separated. This ability to accomplish the objective of speciated isotope dilution measurement on an incomplete specimen is not taught or suggested by the reference.

Finally, dependent claim 33 depends from claim 32 and recites effecting the separation of at least about 5-10 percent of the species. This recites the fact that the invention will work successfully even with such a relatively small portion of the sample.

In summary, it is respectfully submitted that Kingston U.S. Patent 5,414,259 made substantial advancements over the then existing prior art, but does not teach or suggest the

features of the foregoing claims and it is respectfully submitted that claims 1-3 and 5-33 are patentable thereover.

**Claim 4 - Section 103(a)**

This claim was rejected on the basis of Kingston in view of Chen and Ketterer or Kozerski. As this claim has been canceled this rejection has been obviated.

**SUMMARY AND CONCLUSION**

In view of the foregoing it is respectfully submitted that the cancellation of claim 4, coupled with the amendment of claim 1 so as to limit the process to one which involves separating only the portion of the species from the sample in order to effect incomplete separation, as well as the amendment to claim 10 dealing with incomplete separation from other species, coupled with the recitals of the other claims, clearly distinguishes over the prior Kingston patent. As it would appear that the application is now in proper form for issuance of the Notice of Allowance, such action is respectfully requested at an early date.

Respectfully submitted,



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## VERSION WITH MARKINGS TO SHOW CHANGES MADE

**In the Claims:**

Cancel claim 4.

Rewrite claims 1 and 10 as follows.

1. (Twice Amended) A method of speciated isotope dilution measurement of a sample comprising

providing at least one predetermined stable isotope,

preparing a different ~~an~~ isotopic spike for each species to be measured by converting each said stable isotope to a speciated enriched isotope corresponding to the species to be measured in said sample,

spiking the sample containing said species to be measured,

equilibrating said isotopic spiked species with said species to be measured,

separating only at least a portion of said species from said sample in order to effect incomplete separation,

making isotope ratio determinations for each said specie to be measured and mathematically deconvoluting said species concentration while correcting for species conversion, and

effecting said mathematical deconvolution while correcting for said incomplete separation of said species from said sample.

10. (Amended) The method of speciated isotope dilution measurement of Claim 2 ~~4~~ including

employing said process on ~~an incompletely separated a plurality of said species to be measured, and~~

incompletely separating said species from other said species in said sample.